

Figure 1

CD95

>sp|P25445|TNR6_HUMAN Tumor necrosis factor receptor superfamily member 6 precursor (FASL receptor) (Apoptosis-mediating surface antigen FAS) (Apo-1 antigen) (CD95) - Homo sapiens (Human).

```
1                                     60
MLGIWTLPL VLTSVARLSS KSVNAQVTDI NSKGLELRKT VTTVETQNL GLHHDGQFCH
61                                     120
KPCPPGERKA RDCTVNGDEP DCVPCQEGKE YTDKAHFSSK CRRCLCDEG HGLEVEINCT
121                                     180
RTQNTKCRCK PNFFCNSTVC EHCDPCTKCE HGIIECTLT SNTCKEEGS RSNLWLCLL
181                                     240
LLPIPLIVWV KRKEVQKTCR KHRKENQGS EPTLNPETV AINLSDVDLS KYITTIAGVM
241                                     300
TSLQVKGFRV KNGVNEAKID EIKNDNVQDT AEQKVQLLRN WHQLHGKKEA YDTLIKDLKK
301                                     335
ANLCTLAEKI QTIILKDITS DSENSNFRNE IQSLV
```

AA 1-16 Signal peptide (potential)
AA 17-173 extracellular domain (potential)
AA 47-83 CRD1
AA 84-127 CRD2
AA 128-166 CRD3
AA 174-190 transmembrane (potential)
AA 191-335 cytoplasmic (potential)

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Figure 2

IgG1

>sp|P01857|GC1_HUMAN Ig gamma-1 chain C region - Homo sapiens (Human).

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1 60
ASTKGPSVFP LAPSSKSTSG GTAALGCLVK DYFPEPVTVS WNSGALTSGV HTFPAVLQSS
61 120
GLYSLSSVVT VPSSSLGTQT YICNVNHKPS NTKVDKKVEP KSCDKTHTCP PCPAPELLGG
121 180
PSVFLFPPKP KDTLMISRTP EVTCVVVDVS HEDPEVKFNW YVDGVEVHNA KTKPREEQYN
181 240
STYRVVSVLT VLHQDWLNGK EYKCKVSNKA LPAPIEKTIS KAKGQPREPQ VYTLPPSRDE
241 300
LTKNQVSLTC LVKGFYPSDI AVEWESNGQP ENNYKTTTPV LDSDGSFFLY SKLTVDKSRW
301 330
QQGNVFSCSV MHEALHNHYT QKSLSLSPGK
```

AA 99-110 hinge region

AA 111-223 CH2 region

AA 224-330 CH3 region

Variants D239E, L241M

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Figure 4**3. TRAIL-R1**

>sp|000220|T10A_HUMAN Tumor necrosis factor receptor superfamily member 10A precursor (Death receptor 4) (TNF-related apoptosis-inducing ligand receptor 1) (TRAIL receptor-1) (TRAIL-R1) - Homo sapiens (Human).

```
1 60
MAPPPARVHL GAFLAVTPNP GSAASGTEAA AATPSKVWGS SAGRIEPRGG GRGALPTSMG
61 120
QHGPSARARA GRAPGPRPAR EASPRLRVHK TFKFVVVGVL LQVVPSSAAT IKLHDQSIGT
121 180
QQWEHSPLGE LCPPGSHRSE HPGACNRCIE GVGYNASNN LFACLPCTAC KSDEEERSPC
181 240
TTTRNTACQC KPGTFRNDNS AEMCRKCSRG CPRGMVKVD CTPWSDIECV HKESGNGHNI
241 300
WVILVVTLVV PLLLVAVLIV CCCIGSGCGG DPKCMDRVCF WRLGLLRGPG AEDNAHNEIL
301 360
SNADSLSTFV SEQOMESQEP ADLTGVTVQS PGEAQCLLGP AEAEGSQRRR LLVPANGADP
361 420
TETLMLFFDK FANIVPFDSW DQLMRQLDLT KNEIDVVRAG TAGPGDALYA MLMKWVNKTG
421 468
RNASIHTLLD ALERMEERHA KEKIQDLLVD SGKFIYLEDG TGSAVSLE
```

AA 1-23 Signal peptide (potential)
AA 24-239 extracellular domain (potential)
AA 107-145 CRD1
AA 147-188 CRD2
AA 189-229 CRD3
AA 240-262 transmembrane (potential)
AA 263-468 cytoplasmic (potential)

Figure 5

Examples of Trail-R1-Fc fusion proteins with overlapping amino acids:

Trail R1 extracellular domain		huIgG1	
201	239	99	120
AEMCRKCSRG CPRGMVKVKD CTPWSDIECV HKESGNGHN		EP KSCDKTHTCP PCPAPELLGG	
AEMCRKCSRG CPRGMVKVKD CTPWSDIECV HKEP KSCDKTHTCP PCPAPELLGG			
201	239	99	120
AEMCRKCSRG CPRGMVKVKD CTPWSDIECV HKESGNGHN		EP KSCDKTHTCP PCPAPELLGG	
AEMCRKCSRG CPRGMVKVKD CTPWSDIECV HKSCDKTHTCP PCPAPELLGG			
201	239	99	120
AEMCRKCSRG CPRGMVKVKD CTPWSDIECV HKESGNGHN		EP KSCDKTHTCP PCPAPELLGG	
AEMCRKCSRG CPRGMVKVKD CTPWSDIECV HKESCDKTHTCP PCPAPELLGG			
201	239	99	120
AEMCRKCSRG CPRGMVKVKD CTPWSDIECV HKESGNGHN		EP KSCDKTHTCP PCPAPELLGG	
AEMCRKCSRG CPRGMVKVKD CTPWSDIECV HKESGNGHTCP PCPAPELLGG			

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Figure 6

4. TRAIL-R2 (long)

>sp|O14763|T10B_HUMAN Tumor necrosis factor receptor superfamily member 10B precursor (Death receptor 5) (TNF-related apoptosis-inducing ligand receptor 2) (TRAIL receptor-2) (TRAIL-R2) - Homo sapiens (Human).

```
1 60
MEQRGQNAPA ASGARKRHGP GPREARGARP GPRVPKTLVL VVAAVLLLVV AESALITQOD
61 120
LAPQQRAPQ QKRSSPSEGL CPPGHHISED GRDCISCKYG QDYSTHWNDL LFCLRCTRCD
121 180
SGEVELSPCT TTRNTVCQCE EGTFREEDSP EMCRCRTGC PRGMVKVGDC TPWSDIECVH
181 240
KESGTHKSGE APAVEETVTS SPGTPASPCS LSGIIIGVTV AAVVLIVAVF VCKSLLWKKV
241 300
LPYLGKICSG GGGDPERVDR SSQRPGAEDN VLNEIVSILO PTQVPEQEME VQEPAEPTGV
301 360
NMLSPGESEH LLEPAEAERS QRRRLVPAN EGDPTETLRQ CFDDFADLVP FDSWEPLMRK
361 420
LGLMDNEIKV AKAEAAGHRD TLYTMLIKWV NKTGRDASVH TLLDALETLG ERLAKQKIED
421 440
HLLSSGKFMV LEGNADSAMS
```

AA 1-55 Signal peptide
AA 56-210 extracellular domain (potential)
AA 57-94 CRD1
AA 97-137 CRD2
AA 138-178 CRD3
AA 192-206 TAPE
AA 211-231 transmembrane (potential)
AA 232-440 cytoplasmic (potential)

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Figure 7

Examples of Trail-R2(long)-Fc fusion proteins with overlapping amino acids ("repeat" included):

Trail R2 (long) extracellular domain		huIgG1	
171	210	99	120
TPWSDIECVH KESGTKHSGE APAVEETVTS SPGTPASPCS		EP KSCDKTHTCP PCPAPELLGG	
TPWSDIECVH KESGTKHSGE APAVEETVTS SPGTPASPCSCDKTHTCP PCPAPELLGG			
Bevorzugte Ausführung (wie in EP 03006949.6 beschrieben)			
171	210	99	120
TPWSDIECVH KESGTKHSGE APAVEETVTS SPGTPASPCS		EP KSCDKTHTCP PCPAPELLGG	
TPWSDIECVH KESGTKHSGE APAVEETVTS SPGTPASCDKTHTCP PCPAPELLGG			
171	210	99	120
TPWSDIECVH KESGTKHSGE APAVEETVTS SPGTPASPCS		EP KSCDKTHTCP PCPAPELLGG	
TPWSDIECVH KESGTKHSGE APAVEETVTS SPGTPAS KSCDKTHTCP PCPAPELLGG			
171	210	99	120
TPWSDIECVH KESGTKHSGE APAVEETVTS SPGTPASPCS		EP KSCDKTHTCP PCPAPELLGG	
TPWSDIECVH KESGTKHSGE APAVEETVTS SPGTPAS KSCDKTHTCP PCPAPELLGG			
171	210	99	120
TPWSDIECVH KESGTKHSGE APAVEETVTS SPGTPASPCS		EP KSCDKTHTCP PCPAPELLGG	
TPWSDIECVH KESGTKHSGE APAVEETVTS SPGTP KSCDKTHTCP PCPAPELLGG			
171	210	99	120
TPWSDIECVH KESGTKHSGE APAVEETVTS SPGTPASPCS		EP KSCDKTHTCP PCPAPELLGG	
TPWSDIECVH KESGTKHSGE APAVEETVTS SPGTPASCDKTHTCP PCPAPELLGG			
171	210	99	120
TPWSDIECVH KESGTKHSGE APAVEETVTS SPGTPASPCS		EP KSCDKTHTCP PCPAPELLGG	
TPWSDIECVH KESGTKHSGE APAVEETVTS SPGTHTCP PCPAPELLGG			

Figure 8

Examples of Trail-R2(long)-Fc fusion proteins with overlapping amino acids ("repeat" not included):

Trail R2 (long) extracellular domain	huIgG1
171191 TPWSDIECVH KESGTKHSGE A	99120 EP KSCDKTHTCP PCPAPELLGG
TPWSDIECVH KESGTKHSGE P KSCDKTHTCP PCPAPELLGG	
171191 TPWSDIECVH KESGTKHSGE A	99120 EP KSCDKTHTCP PCPAPELLGG
TPWSDIECVH KESGTKSCDKTHTCP PCPAPELLGG	
171191 TPWSDIECVH KESGTKHSGE A	99120 EP KSCDKTHTCP PCPAPELLGG
TPWSDIECVH KESGTKSCDKTHTCP PCPAPELLGG	
171191 TPWSDIECVH KESGTKHSGE A	99120 EP KSCDKTHTCP PCPAPELLGG
TPWSDIECVH KESGTHTCP PCPAPELLGG	
171191 TPWSDIECVH KESGTKHSGE A	99120 EP KSCDKTHTCP PCPAPELLGG
TPWSDIECVH KESGTKHTCP PCPAPELLGG	

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Figure 9**5. TRAIL-R2 (short)**

>sp|O14763|T10B_HUMAN Tumor necrosis factor receptor superfamily member 10B precursor (Death receptor 5) (TNF-related apoptosis-inducing ligand receptor 2) (TRAIL receptor-2) (TRAIL-R2) - Homo sapiens (Human).

```
1                                     60
MEQRGQNAPA ASGARKRHGP GPREARGARP GPRVPKTLVL VVAAVLLLVV AESALITQOD
61                                     120
LAPQQRAAPQ QKRSSPSEGL CPPGHHISED GRDCISCKYG QDYSTHWNDL LFCLRCTRCD
121                                     180
SGEVELSPCT TTRNTVCQCE EGTFREEDSP EMCRKCRTGC PRGMVKVGDC TPWSDIECVH
181                                     240
KESGIIIGVT VAAVVLIVAV FVCKSLLWKK VLPYLGICS GGGGDPERVD RSSQRPGAED
241                                     300
NVLNEIVSIL OPTQVPEQEM EVQEPAEPTG VNMLSPGESE HLEPAEAER SQRRRLVPA
301                                     360
NEGDPTETLR QCFDDFADLV PFDSWEPLMR KLGLMDNEIK VAKAEAAGHR DTLYTMLIKW
361                                     411
VNKTGRDASV HTLLDALETG GERLAKQKIE DHLLSSGKFM YLEGNADSAM S
```

AA 1-55 Signal peptide
AA 56-184 extracellular domain (potential)
AA 57-94 CRD1
AA 97-137 CRD2
AA 138-178 CRD3
AA 213-202 transmembrane (potential)
AA 203-411 cytoplasmic (potential)

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Figure 10

Examples of Trail-R2(short)-Fc fusion proteins with overlapping amino acids:

Trail-R2 (short) extracellular domain		huIgG1	
151	184	99	120
EMCRKCRTGC PRGMVKVGDC TPWSDIECVH KESG		EP KSCDKTHTCP PCPAPELLGG	
EMCRKCRTGC PRGMVKVGDC TPWSDIECVH KEP KSCDKTHTCP PCPAPELLGG			
151	184	99	120
EMCRKCRTGC PRGMVKVGDC TPWSDIECVH KESG		EP KSCDKTHTCP PCPAPELLGG	
EMCRKCRTGC PRGMVKVGDC TPWSDIECVH KSCDKTHTCP PCPAPELLGG			
151	184	99	120
EMCRKCRTGC PRGMVKVGDC TPWSDIECVH KESG		EP KSCDKTHTCP PCPAPELLGG	
EMCRKCRTGC PRGMVKVGDC TPWSDIECVH KESCDKTHTCP PCPAPELLGG			
151	184	99	120
EMCRKCRTGC PRGMVKVGDC TPWSDIECVH KESG		EP KSCDKTHTCP PCPAPELLGG	
EMCRKCRTGC PRGMVKVGDC TPWSDIECVHTCP PCPAPELLGG			

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Figure 11**6. TRAIL-R3**

>sp|O14798|T10C_HUMAN Tumor necrosis factor receptor superfamily member 10C precursor (Decoy receptor 1) (DcR1) (Decoy TRAIL receptor without death domain) (TNF- related apoptosis-inducing ligand receptor 3) (TRAIL receptor-3) (TRAIL-R3) (Trail receptor w

```
1 60
MARIPKTLKF VVVIVAVLLP VLAYSATTAR QEEVPQQTVA PQQQRHSFKG EECFAGSHRS
61 120
EHTGACNPCT EGVDTYNASN NEPSCFPCTV CKSDQKHKSS CTMTRDTVQC CKEGTFRNEN
121 180
SPEMCRKCSR CPSGEVQVSN CTSWDDIQCV EEFGANATVE TPAAEETMNT SPGTPAPAAE
181 240
ETMNTSPGTP APAAEETMTT SPGTPAPAAE ETMTTSPGTP APAAEETMTT SPGTPASSHY
241 259
LSCTIVGIIV LIVLLIVFV
```

AA 1-23 Signal peptide
AA 24-236 extracellular domain
AA 29-66 CRD1
AA 69-109 CRD2
AA 110-149 CRD3
AA 162-236 5 x 15 AA tandem tape repeats
AA 237-259 removed in mature form (potential)

Figure 12

Examples of Trail-R3-Fc fusion proteins with overlapping amino acids
("repeats" included):

Trail-R3 extracellular domain	huIgG1
201236 SPGTPAPAAE ETMTTSPGTP APAAEETMTT SPGTPA	99120 EP KSCDKTHTCP PCPAPELLGG
SPGTPAPAAE ETMTTSPGTP APAAEETMTT SPGTP KSCDKTHTCP PCPAPELLGG	
201236 SPGTPAPAAE ETMTTSPGTP APAAEETMTT SPGTPA	99120 EP KSCDKTHTCP PCPAPELLGG
SPGTPAPAAE ETMTTSPGTP APAAEETMTT SP KSCDKTHTCP PCPAPELLGG	
201236 SPGTPAPAAE ETMTTSPGTP APAAEETMTT SPGTPA	99120 EP KSCDKTHTCP PCPAPELLGG
SPGTPAPAAE ETMTTSPGTP APAAEETMTT SCDKTHTCP PCPAPELLGG	
201236 SPGTPAPAAE ETMTTSPGTP APAAEETMTT SPGTPA	99120 EP KSCDKTHTCP PCPAPELLGG
SPGTPAPAAE ETMTTSPGTP APAAEETMTT SPGHTCP PCPAPELLGG	
201236 SPGTPAPAAE ETMTTSPGTP APAAEETMTT SPGTPA	99120 EP KSCDKTHTCP PCPAPELLGG
SPGTPAPAAE ETMTTSPGTP APAAEETMTT HTCP PCPAPELLGG	
201236 SPGTPAPAAE ETMTTSPGTP APAAEETMTT SPGTPA	99120 EP KSCDKTHTCP PCPAPELLGG
SPGTPAPAAE ETMTTSPGTP APAAEETMT HTCP PCPAPELLGG	

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Figure 13

Examples of Trail-R3-Fc fusion proteins with overlapping amino acids
("repeats" not included):

Trail-R3 extracellular domain	huIgG1
121 161 SPEMCRKCSR CPSGEVQVSN CTSWDDIQCV EEFGANATVE T	99 120 EP KSCDKTHTCP PCPAPELLGG
SPEMCRKCSR CPSGEVQVSN CTSWDDIQCV EEFGANATVEP KSCDKTHTCP PCPAPELLGG	
121 161 SPEMCRKCSR CPSGEVQVSN CTSWDDIQCV EEFGANATVE T	99 120 EP KSCDKTHTCP PCPAPELLGG
SPEMCRKCSR CPSGEVQVSN CTSWDDIQCV EP KSCDKTHTCP PCPAPELLGG	
121 161 SPEMCRKCSR CPSGEVQVSN CTSWDDIQCV EEFGANATVE T	99 120 EP KSCDKTHTCP PCPAPELLGG
SPEMCRKCSR CPSGEVQVSN CTSWDDIQCV EP KSCDKTHTCP PCPAPELLGG	
121 161 SPEMCRKCSR CPSGEVQVSN CTSWDDIQCV EEFGANATVE T	99 120 EP KSCDKTHTCP PCPAPELLGG
SPEMCRKCSR CPSGEVQVSN CTSWDDIQCV EEFGANATVE HTCP PCPAPELLGG	
121 161 SPEMCRKCSR CPSGEVQVSN CTSWDDIQCV EEFGANATVE T	99 120 EP KSCDKTHTCP PCPAPELLGG
SPEMCRKCSR CPSGEVQVSN CTSWDDIQCV EEFGANATHTCP PCPAPELLGG	

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Figure 14**7. TRAIL-R4**

>sp|Q9UBN6|T10D_HUMAN Tumor necrosis factor receptor superfamily member 10D precursor (Decoy receptor 2) (DcR2) (TNF-related apoptosis-inducing ligand receptor 4) (TRAIL receptor-4) (TRAIL-R4) (TRAIL receptor with a truncated death domain) - Homo sapiens

```
1 60
MGLWGQSVPT ASSARAGRYP GARTASGTRP WLLDPKILKF VVFIVAVLLP VRVDSATIPR
61 120
QDEVPOQTVA PQQORRSLKE EECFAGSHRS EYTGACNPCT EGVDYTIASN NLPSCLLCTV
121 180
CKSGQTNKSS CTTTRDTVCQ CEKGSFQDKN SPEMCRTCRT GCPRGMVKVS NCTPRSDIKC
181 240
KNESAASSTG KTPAAEETVT TILGMLASPY HYLIIIVVLV IILAVVVVGF SCRKKFISYL
241 300
KGICSGGGGG PERVHRVLFR RRSCPSRVPG AEDNARNETL SNRYLOPTQV SEQEIQGQEL
301 360
AELTGVTVES PEEPQRLLEQ AEAEGCQRRR LLVPVNDADS ADISTLLDAS ATLEEGHAK
361 386
TIQDQLVGSE KLFYEEDEAG SATSCL
```

AA 1-55 signal peptide
AA 56-211 extracellular domain (potential)
AA 58-97 CRD1
AA 98-139 CRD2
AA 140-180 CRD3
AA 212-232 transmembrane (potential)
AA 233-386 cytoplasmic (potential)

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Figure 15

Examples of Trail-R4-Fc fusion proteins with overlapping amino acids:

Trail-R4 extracellular domain		huIgG1	
171	211	99	120
NCTPRSDIKC KNESAASSTG KTPAAEETVT TILGMLASPY H		EP KSCDKTHTCP PCPAPELLGG	
NCTPRSDIKC KNESAASSTG KTPAAEETVT TILGMLAS KSCDKTHTCP PCPAPELLGG			
171	211	99	120
NCTPRSDIKC KNESAASSTG KTPAAEETVT TILGMLASPY H		EP KSCDKTHTCP PCPAPELLGG	
NCTPRSDIKC KNESAASSTG KTPAAEETVT TILGMLASCDKTHTCP PCPAPELLGG			
171	211	99	120
NCTPRSDIKC KNESAASSTG KTPAAEETVT TILGMLASPY H		EP KSCDKTHTCP PCPAPELLGG	
NCTPRSDIKC KNESAASSTG KTPAAEETVT THTCP PCPAPELLGG			
171	211	99	120
NCTPRSDIKC KNESAASSTG KTPAAEETVT TILGMLASPY H		EP KSCDKTHTCP PCPAPELLGG	
NCTPRSDIKC KNESAASSTG KTPAAEETVT TILGMLASPY HTCP PCPAPELLGG			

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Figure 16**1. TNF-R1**

>sp|P19438|TR1A_HUMAN Tumor necrosis factor receptor superfamily member 1A precursor (p60) (TNF-R1) (TNF-RI) (p55) (CD120a) [Contains: Tumor necrosis factor binding protein 1 (TBPI)] - Homo sapiens (Human).

```
1 60
MGLSTVPDLL LPLVLLELLV GIYPSGVIGL VPHLGDREKR DSVCPQGKYI HPQNNsicCT
61 120
KCHKGTYLYN DCPGPGQDTD CRECESGSFT ASENHLRHCL SCSKCRKEMG QVEISSCTVD
121 180
RDTVCGCRKN QYRHYWSENL FQCFNCSLCL NGTVHLSCQE KQNTVCTCHA GFFLRENECV
181 240
SCSNCKKSLE CTKLCLPQIE NVKGTEDSGT TVLLPLVIFF GLCLLSLLFI GLMYRYQRWK
241 300
SKLYSIVCGK STPEKEGELE GTTTKPLAPN PSFSPTPGFT PTLGFSPVPS STFTSSSTYT
301 360
PGDCPNFAAP RREVAPPYQG ADPILATALA SDPIPNPLQK WEDSAHKPQS LDTDDPATLY
361 420
AVVENVPPLR WKEFVRLGL SDHEIDRLEL QNGRCLREAQ YSMLATWRRR TPRREATLEL
421 455
LGRVLRDMDL LGCLEDIEEA LCGPAALPPA PSLLR
```

AA 1-21 Signal peptide
AA 22-211 extracellular domain (potential)
AA 43-82 CRD1
AA 83-125 CRD2
AA 126-166 CRD3
AA 167-196 CRD4
AA 212-234 transmembrane (potential)
AA 235-455 cytoplasmic (potential)

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Figure 17

Examples of TNF-R1-Fc fusion proteins with overlapping amino acids:

TNF-R1 extracellular domain		huIgG1	
171	211	99	120
GFFLRENECV SCSNCKKSLE CTKLCLPQIE NVKGTE D SGT T		EP KSCDKTHTCP PCPAPELLGG	
GFFLRENECV SCSNCKKSLE CTKLCLPQIE NVKGTE P KSCDKTHTCP PCPAPELLGG			
171	211	99	120
GFFLRENECV SCSNCKKSLE CTKLCLPQIE NVK R GTEDSGT T		EP R KSCDKTHTCP PCPAPELLGG	
GFFLRENECV SCSNCKKSLE CTKLCLPQIE NV K RSCDKTHTCP PCPAPELLGG			
171	211	99	120
GFFLRENECV SCSNCKKSLE CTKLCLPQIE NV K GTEDSGT T		EP KSCD K THTCP PCPAPELLGG	
GFFLRENECV SCSNCKKSLE CTKLCLPQIE NV K THTCP PCPAPELLGG			
171	211	99	120
GFFLRENECV SCSNCKKSLE CTKLCLPQIE NVKGTE D SGT T		EP K S CDKTHTCP PCPAPELLGG	
GFFLRENECV SCSNCKKSLE CTKLCLPQIE NVKGTE D SCDKTHTCP PCPAPELLGG			
171	211	99	120
GFFLRENECV SCSNCKKSLE CTKLCLPQIE NVKGTE D SGT T		EP KSCD K THTCP PCPAPELLGG	
GFFLRENECV SCSNCKKSLE CTKLCLPQIE NVKGTE D KTHTCP PCPAPELLGG			
171	211	99	120
GFFLRENECV SCSNCKKSLE CTKLCLPQIE NVKGTE D SGT T		EP KSCDK T HTCP PCPAPELLGG	
GFFLRENECV SCSNCKKSLE CTKLCLPQIE NVKGTE D SGT T HTCP PCPAPELLGG			
171	211	99	120
GFFLRENECV SCSNCKKSLE CTKLCLPQIE NVKGTE D SGT T		EP KSCDK T HTCP PCPAPELLGG	
GFFLRENECV SCSNCKKSLE CTKLCLPQIE NVKGTE D SGT T HTCP PCPAPELLGG			

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Figure 18**2. TNF-R2**

>sp|P20333|TR1B_HUMAN Tumor necrosis factor receptor superfamily member 1B precursor (Tumor necrosis factor receptor 2) (p80) (TNF-R2) (p75) (CD120b) (Etanercept) [Contains: Tumor necrosis factor binding protein 2 (TBPII)] - Homo sapiens (Human).

```

1                                     60
MAPVAVWAAL AVGLELWAAA HALPAQVAFT PYAPEPGSTC RLREYYDQTA QMCCSKCSPG
61                                     120
QHAKVFCTKT SDTVCDSCED STYTQLWNWV PECLSCGSRC SSDQVETQAC TREQNRICTC
121                                     180
RPGWYCALSK QEGCRLCAPL RKCRPGFGVA RPGTETSDVV CKPCAPGTFS NTTSTSDICR
181                                     240
PHQICNVVAI PGNASMDAVC TSTSPTRSMA PGAVHLPOPV STRSQHTOPT PEPSTAPSTS
241                                     300
FLLPMGSPSP AEGSTIGDFAL PVGLIVGVTA LGLLIIGVVN CVIMTQVKKK PLCLQREAKV
301                                     360
PHLPADKARG TQGPEQQHLL ITAPSSSSSS LESSASALDR RAPTRNQPQA PGVEASGAGE
361                                     420
ARASTGSSDS SPGGHGTQVN VTCIVNVCSS SDHSSQCSSQ ASSTMGDTDS SPSESPKDEQ
421                                     461
VPFSKEECAAF RSQLETPETL LGSTEEKPLP LGVPDAGMKP S

```

AA 1-22 Signal peptide
AA 23-257 extracellular domain (potential)
AA 39-76 CRD1
AA 77-118 CRD2
AA 119-162 CRD3
AA 163-201 CRD4
AA 258-287 transmembrane (potential)
AA 288-461 cytoplasmic (potential)

Figure 19

Examples of TNF-R2-Fc fusion proteins with overlapping amino acids:

TNF-R2 extracellular domain		huIgG1	
221	257	99	120
STRSQHTQPT PEPSTAPSTS FLLPMGPSPP AEGSTGD		EP KSCDKTHTCP PCPAPELLGG	
STRSQHTQPT PEPSTAPSTS FLLPMGPSPP AEP KSCDKTHTCP PCPAPELLGG			
221	257	99	120
STRSQHTQPT PEPSTAPSTS FLLPMGPSPP AEGSTGD		EP KSCDKTHTCP PCPAPELLGG	
STRSQHTQPT PEPSTAPSTS FLLPMGPSPP KSCDKTHTCP PCPAPELLGG			
221	257	99	120
STRSQHTQPT PEPSTAPSTS FLLPMGPSPP AEGSTGD		EP KSCDKTHTCP PCPAPELLGG	
STRSQHTQPT PEPSTAPSTS FLLPMGPSPP KSCDKTHTCP PCPAPELLGG			
221	257	99	120
STRSQHTQPT PEPSTAPSTS FLLPMGPSPP AEGSTGD		EP KSCDKTHTCP PCPAPELLGG	
STRSQHTQPT PEPSTAPSTS FLLPMGPSPP AEGSCDKTHTCP PCPAPELLGG			
221	257	99	120
STRSQHTQPT PEPSTAPSTS FLLPMGPSPP AEGSTGD		EP KSCDKTHTCP PCPAPELLGG	
STRSQHTQPT PEPSTAPSTS FLLPMGPSPP KSCDKTHTCP PCPAPELLGG			
221	257	99	120
STRSQHTQPT PEPSTAPSTS FLLPMGPSPP AEGSTGD		EP KSCDKTHTCP PCPAPELLGG	
STRSQHTQPT PEPSTAPSTS FLLPMGPSPP AEGSTGDKTHTCP PCPAPELLGG			
221	257	99	120
STRSQHTQPT PEPSTAPSTS FLLPMGPSPP AEGSTGD		EP KSCDKTHTCP PCPAPELLGG	
STRSQHTQPT PEPSTAPSTS FLLPMGPSPP AEGSTHTCP PCPAPELLGG			